4

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/600,493	07/18/2000	Jack Wands	MGH-0026	3498

23377 7590 07/28/2005

WOODCOCK WASHBURN LLP
ONE LIBERTY PLACE, 46TH FLOOR
1650 MARKET STREET
PHILADELPHIA, PA 19103

EXAMINER	
LIETO, LOUIS D	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/600,493	WANDS ET AL.	
	Examiner	Art Unit	
	Louis D. Lieto	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,6-8,17,20-28 and 48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,6-8,17,20-28 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 4/25/2005 is acknowledged. Claims 4, 6-8, 17, 20-28, and 48 are pending in the instant application. Applicant canceled claim 47, and amended claim 6 and 42. The sections of title 35 U.S.C not included in this office action can be found in a previous office action. An action on the merits follows.

Claim Objections

Claim 48 is newly objected to as being dependent upon a cancelled base claim. Appropriate correction is required. This new objection was necessitated by applicant's cancellation of claim 47.

Claim Rejections - 35 USC § 112

The rejection of claims 14, 6, 7, 8, 17, and 20-28 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn. Applicant's amendments to the claims, see the reply, filed on 4/25/2005, with respect to failure to comply with the written description requirement, have been fully considered and are persuasive. The rejection of record has been withdrawn.

The rejection of claims 4, 6, 7, 8, 17, 20-28 and 48 under 35 U.S.C. 112, first paragraph is maintained, because the specification, while being enabling for a recombinant nucleic acid molecule consisting of a nucleotide sequence encoding hepatitis C virus nonstructural proteins NS3, NS4 and NS5, wherein said nucleotide sequence is operably linked to regulatory elements,

said regulatory elements comprising a promoter, enhancer, polyadenylation sequence, and at most the 9 most 3' nucleotides of the 5'UTR of a hepatitis C virus, and a method of inducing an immune response by administration of said recombinant nucleic acid molecule, does not reasonably provide enablement for a recombinant nucleic acid molecule consisting of a nucleotide sequence encoding hepatitis C virus nonstructural proteins NS3, NS4 and NS5, wherein said nucleotide sequence is operably linked to regulatory elements, said regulatory elements comprising a promoter, enhancer, polyadenylation sequence, and a 5' untranslated region from any gene The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicant's arguments filed 4/25/2005 have been fully considered but they are not persuasive. The previous office action identified the following issue of record: failure of the specification to provide an enabling disclosure for making or using a recombinant nucleic acid molecule consisting of a nucleotide sequence encoding hepatitis c virus NS3, NS4, and NS5 proteins, operably linked to a promoter, enhancer, polyA and the 5' UTR of the hepatitis C virus or any other gene. Applicant's amendment to the claims so that the read on only a 5'UTR region of a hepatitis C virus obviates the elements of the rejection that refer to a 5' UTR from any other gene.

Response to Arguments

Applicant's arguments filed 4/25/2005 have been fully considered but they are not persuasive. Applicant's argue that the reference of Selby et al. does not lead one to the

conclusion that inclusion of the 5' UTR does not lead one to the conclusion "that it is not clear whether the claimed construct would produce sufficient protein to produce an immune response." Applicant cites Tokushige et al. in support of their argument that a construct with an intact HCV 5'UTR provides sufficient intracellular expression of HCV core protein to produce immune reactive HCV core protein detectable on a western blot (pg. 15, Fig. 1B). It is noted that Fig. 1B shows western blots of HCV core protein after transfection of 3 different cell lines with plasmids encoding the HCV core protein with (pHCV 4-2) or without (pHCV 2-2) the HCV 5' UTR. In RD cells and G8 cells the amount of protein produced from the pHCV 4-2 is nearly undetectable, only in the HuH7 cell line does pHCV 4-2 produce any significant amounts of detectable HCV core protein. Overall the clear implication of Fig 1B is that plasmids containing the 5'UTR of HCV produce significantly less HCV core protein in comparison to plasmids that do not contain the HCV 5' UTR. Further, Fig. 5 clearly shows that pHCV 4-2 has no effect on tumor weight in comparison to a mock transfection (pg. 18). This indicates that it is disadvantageous to include the entire 5'UTR of HCV in an expression vector designed to induce an immune response. Applicant further argues that the absolute quantity of protein produced by a DNA expression vector does not necessarily correlate with the level of immune response in a subject. However applicant's argument is irrelevant since the only disclosed utility of the recombinant nucleic acid molecule and a method of using the recombinant nucleic acid molecule is to induce protective immunity. Applicant has not disclosed in the specification or provided any evidence to suggest that the claimed vector can produce any level of immune response in a mammalian subject, much less protective immunity. Based on the art cited in the office action of 1/25/2005 and Tokushige et al., the skilled practitioner would not predict that a construct

containing the 5' UTR region of HCV would produce sufficient protein to produce a protective immune response in a mammal.

Next applicant states that the reference of Yoo et al. is of record and cites it in support of their contention that their invention is enabled as presently claimed. However, a review of references cited by the office during prosecution or submitted by applicant in an Information Disclosure Statement does not indicate that this reference has been submitted to the office or is present in the record. The only reference to Yoo et al. that was identified by the examiner was in the declaration of Jack Wands filed on 1/24/2003. If applicant wishes to make this reference of record they should submit it in an Information Disclosure Statement. Since the reference does not appear to be present in the record, or provided by applicant it was not considered in its entirety. Given the age of the reference only the abstract is readily available. A review of the abstract of Yoo et al. indicates that it fails to provide support for applicant's position that a construct containing the entire HCV 5' UTR is enabled. Specifically, Yoo et al. states that "(1) the full-length 5' UTR of HCV-1 RNA is translationally inactive...[and] (2) an efficient *cis*-acting element which represses translation is found at the 5' terminus." {Yoo et al. (1992) Virology 191:889-899; Abstract}. Based on the disclosure of Yoo et al. the skilled practitioner would not predict that a construct containing the 5' UTR region of HCV would produce sufficient protein to produce a protective immune response in a mammal.

Further, the quoted paragraph from Jack Woods is argues that "one skilled in the art would be able to operably link the 5'UTR of HCV to a recombinant plasmid for proteins", such as HCV NS proteins. The core of the enablement rejection is not that applicant could not make the claimed plasmid. The basis of rejection is that the skilled practitioner would be unable to

predict that said plasmid would produce sufficient protein to produce an immune response. In fact given the structural analysis of the 5' UTR provided in the previous office action and the references of Tokushige et al. and Yoo et al. the skilled practitioner would predict that a construct containing any length of the 5' UTR of HCV, except at most the 9 most 3' nucleotides of the 5'UTR, which encode the Kozak sequence, would most likely produce lower levels of protein than a construct lacking the 5' UTR of HCV and thus be less likely to produce a protective immune response in a mammal.

Applicant argues that the examiner has no reason to doubt the objective truth of the statements contained in the application and cites In re Manocchi, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971). The examiner has not argued that applicant's specification is untrue, instead the examiner has argued that the specification does not provide support for the claimed invention. The lack of working examples and the teachings in the art combine to indicate that the skilled practitioner would not predict that the claimed invention could be used for the intended use. It is noted that the unpredictability of a particular art area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). It is also well established in case law that the specification must teach those of skill in the art how to make and how to use the invention as broadly claimed. In re Goodman, 29 USPQ2d at 2013 (Fed. Cir. 1994), citing In re Vaeck, 20 USPQ2d at 1445 (Fed. Cir. 1991). In the instant case, there is no evidence in the specification which supports that any length fragment of the 5'UTR of HCV could be used in the claimed construct and produce sufficient protein to produce a protective immune response in a mammal.

Finally, it is noted that applicant has not addressed the examiner's previous arguments set forth in the office action of 1/25/2005 about the multiple pre-mature Start codons present in the 5' UTR and the negative effect such codons are known to have on the efficiency of translation. The rejection is maintained for the reasons of record as stated above and in the office action of 1/25/2005.

No Claims Allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571)-272-0735. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Patent applicants with problems or questions regarding electronic images that can be viewed in the PAIR can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Dr. Louis D. Lieto
Patent Examiner
Art Unit 1632

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP ~~1800~~ 1630